

## PRIOR AUTHORIZATION POLICY

- POLICY:** Oncology – Everolimus Products Prior Authorization Policy
- Afinitor<sup>®</sup> (everolimus tablets – Novartis, generic)
  - Afinitor Disperz<sup>®</sup> (everolimus tablets for oral suspension – Novartis)
  - Torpenz<sup>™</sup> (everolimus tablets – Upsher-Smith)

**REVIEW DATE:** 03/06/2024; selected revision 07/03/2024

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### OVERVIEW

Afinitor, a kinase inhibitor, is indicated for the following uses:<sup>1</sup>

- **Breast cancer**, treatment of advanced hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative disease in combination with exemestane, after failure of treatment with letrozole or anastrozole in postmenopausal women.
- **Neuroendocrine tumors (NET)**, treatment of progressive disease of pancreatic origin and progressive, well-differentiated, non-functional NET of gastrointestinal or lung origin that are unresectable, locally advanced, or metastatic in adults. Limitation of Use: Afinitor is not indicated for the treatment of patients with functional carcinoid tumors.
- **Renal cell carcinoma**, treatment of advanced disease after failure of treatment with sunitinib or sorafenib in adults.
- **Tuberous sclerosis complex (TSC)-associated renal angiomyolipoma**, treatment of adults not requiring immediate surgery.
- **TSC-associated subependymal giant cell astrocytoma (SEGA)**, treatment of patients  $\geq 1$  year of age who require therapeutic intervention but cannot be curatively resected.

Afinitor Disperz, a kinase inhibitor, is indicated for the following uses:<sup>1</sup>

- **TSC-associated SEGA**, treatment of patients  $\geq 1$  year of age who require therapeutic intervention but cannot be curatively resected.
- **TSC-associated partial-onset seizures**, adjunctive treatment of patients  $\geq 2$  years of age.

Torpenz, a kinase inhibitor, is indicated for the following uses:<sup>2</sup>

- **Breast cancer**, treatment of advanced HR+, HER2-negative disease in combination with exemestane, after failure of treatment with letrozole or anastrozole in postmenopausal women.
- **TSC-associated renal angiomyolipoma**, treatment of adults not requiring immediate surgery.
- **TSC-associated SEGA**, treatment of patients  $\geq 1$  year of age who require therapeutic intervention but cannot be curatively resected.

Of note, Zortress<sup>®</sup> (everolimus tablets) is indicated in combination with other drugs for prophylaxis of organ rejection in adults undergoing kidney or liver transplant.<sup>3</sup> The tablet strengths and dosing are different for Zortress and Afinitor. Zortress is not targeted in this policy.

### Guidelines

The National Comprehensive Cancer Network (NCCN) Compendium recommends use of everolimus for the indications listed in the FDA-Approved Indications and Other Uses with Supportive Evidence sections.<sup>4</sup>

### POLICY STATEMENT

03/06/2024

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Prior Authorization is recommended for prescription benefit coverage of everolimus products. All approvals are provided for the duration noted below. In the clinical criteria, as appropriate, an asterisk (\*) is noted next to the specified gender. In this context, the specified gender is defined as follows: a woman is defined as an individual with the biological traits of a woman, regardless of the individual's gender identity or gender expression; men are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression.

**Automation:** None.

## **RECOMMENDED AUTHORIZATION CRITERIA**

Coverage of everolimus products is recommended in those who meet one of the following criteria:

### **FDA-Approved Indications**

- 1. Breast Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, F, and G):
  - A)** Patient is  $\geq 18$  years of age; AND
  - B)** Patient has recurrent or metastatic, hormone receptor positive (HR+) [i.e., estrogen receptor-positive {ER+} and/or progesterone receptor-positive {PR+}] disease; AND
  - C)** Patient has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
  - D)** Patient has tried at least one prior endocrine therapy (e.g., anastrozole, letrozole, or tamoxifen); AND
  - E)** Patient meets ONE of the following conditions (i or ii):
    - i.** Patient is a postmenopausal woman\* or a man\*<sup>\*</sup>; OR
    - ii.** Patient is a pre/perimenopausal woman\* and meets ONE of the following (a or b):
      - a)** Patient is receiving ovarian suppression/ablation with a gonadotropin-releasing hormone (GnRH) agonist; OR  
Note: Examples of a GnRH agonist include leuprolide acetate, Lupron Depot (leuprolide acetate intramuscular injection), Trelstar (triptorelin pamoate intramuscular injection), Zoladex (goserelin acetate subcutaneous implant).
      - b)** Patient has had surgical bilateral oophorectomy or ovarian irradiation; AND
  - F)** Patient meets ONE of the following conditions (i or ii):
    - i.** The medication will be used in combination with exemestane and the patient meets ONE of the following (a or b):
      - a)** Patient is a man\* and the patient is receiving a gonadotropin-releasing hormone (GnRH) analog; OR  
Note: Examples of a GnRH analog include leuprolide acetate, Lupron Depot (leuprolide acetate intramuscular injection), Trelstar (triptorelin pamoate intramuscular injection), Zoladex (goserelin acetate subcutaneous implant), Firmagon (degarelix acetate subcutaneous injection), and Orgovyx (relugolix tablet).
      - b)** Patient is a woman\*<sup>\*</sup>; OR
    - ii.** The medication will be used in combination with fulvestrant or tamoxifen; AND
  - G)** Patient has not had disease progression while on everolimus.

\*Refer to the Policy Statement.

- 2. Neuroendocrine Tumors of the Pancreas, Gastrointestinal Tract, Lung, and Thymus (Carcinoid Tumors).** Approve for 1 year if the patient is  $\geq 18$  years of age.
- 3. Renal Cell Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):

- A) Patient is  $\geq 18$  years of age; AND
- B) Patient has relapsed or Stage IV disease; AND
- C) Patient meets ONE of the following (i or ii):
  - i. Patient has non-clear cell disease; OR
  - ii. Patient meets both of the following (a and b):

- a) Patient has clear cell disease; AND

- b) Patient has tried at least one prior systemic therapy.

Note: Examples of prior systemic therapy include the following products: Inlyta (axitinib tablets), Lenvima (lenvatinib capsules), Cabometyx (cabozantinib tablets), Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), pazopanib, sunitinib.

- 4. **Tuberous Sclerosis Complex-Associated Renal Angiomyolipoma.** Approve for 1 year.
- 5. **Tuberous Sclerosis Complex-Associated Subependymal Giant Cell Astrocytoma (SEGA).** Approve for 1 year if therapeutic intervention is required but SEGA cannot be curatively resected.
- 6. **Tuberous Sclerosis Complex-Associated Partial Onset Seizures.** Approve for 1 year.

#### Other Uses with Supportive Evidence

- 7. **Endometrial Carcinoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
  - A) Patient is  $\geq 18$  years of age; AND
  - B) The medication will be used in combination with letrozole.
- 8. **Gastrointestinal Stromal Tumors.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
  - A) Patient is  $\geq 18$  years of age; AND
  - B) Patient has tried each of the following (i, ii, iii, and iv):
    - i. One of imatinib or Ayvakit (avapritinib tablets); AND
    - ii. One of sunitinib or Sprycel (dasatinib tablets); AND
    - iii. Stivarga (regorafenib tablets); AND
    - iv. Qinlock (ripretinib tablets); AND
  - C) The medication will be used in combination with imatinib, sunitinib, or Stivarga (regorafenib tablets).
- 9. **Histiocytic Neoplasm.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
  - A) Patient is  $\geq 18$  years of age; AND
  - B) Patient meets ONE of the following (i, ii, or iii):
    - i. Patient has Langerhans cell histiocytosis; OR
    - ii. Patient has Erdheim-Chester disease; OR
    - iii. Patient has Rosai-Dorfman disease; AND
  - C) Patient has a *PIK3CA* mutation.
- 10. **Classic Hodgkin Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B and C):
  - A) Patient is  $\geq 18$  years of age; AND
  - B) Patient has relapsed or refractory disease; AND
  - C) Patient has tried at least three prior lines of chemotherapy.

Note: Examples of therapy include one or more of the following drugs: bendamustine, carboplatin, cisplatin, cytarabine, etoposide, doxorubicin, gemcitabine, ifosfamide, vinorelbine, Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion).

**11. Meningioma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

- A) Patient is  $\geq 18$  years of age; AND
- B) Patient has recurrent or progressive disease; AND
- C) Patient meets BOTH of the following: (i and ii):
  - i. Patient has surgically inaccessible disease; AND
  - ii. Radiation therapy is not possible.
- D) The medication will be used in combination with a somatostatin analogue.

Note: Example of somatostatin analogue includes: octreotide.

**12. Soft Tissue Sarcoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient is  $\geq 18$  years of age; AND
- B) Patient has ONE of the following conditions (i or ii):
  - i. Perivascular epithelioid cell tumor (PEComa); OR
  - ii. Recurrent angiomyolipoma/lymphangiomyomatosis.

**13. Thymomas and Thymic Carcinomas.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient is  $\geq 18$  years of age; AND
- B) Patient meets ONE of the following (i or ii):
  - i. Patient has tried chemotherapy; OR  
Note: Examples are cisplatin, doxorubicin, and cyclophosphamide; cisplatin plus etoposide; carboplatin plus paclitaxel.
  - ii. Patient cannot tolerate chemotherapy.

**14. Thyroid Carcinoma, Differentiated.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):

- A) Patient is  $\geq 18$  years of age; AND
- B) Patient has differentiated thyroid carcinoma; AND  
Note: Examples of differentiated thyroid carcinoma include papillary, follicular, and oncocytic thyroid carcinoma.
- C) The disease is refractory to radioactive iodine therapy.

**15. Uterine Sarcoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C and D):

- A) Patient is  $\geq 18$  years of age; AND
- B) Patient has advanced, recurrent, metastatic, or inoperable disease; AND
- C) Patient has a perivascular epithelioid cell tumor (PEComa); AND
- D) Patient has tried at least one systemic regimen.  
Note: Examples of systemic regimen include doxorubicin, docetaxel, gemcitabine, ifosfamide, dacarbazine.

**16. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):

- A) Patient is  $\geq 18$  years of age; AND
- B) Patient meets ONE of the following (i or ii):
  - i. Patient has not responded to primary therapy; OR

Note: Examples of primary therapy are bortezomib, dexamethasone, and rituximab; bendamustine and rituximab; cyclophosphamide, rituximab and dexamethasone; Imbruvica (ibrutinib capsules, tablets, and oral solution); and Brukinsa (zanubrutinib capsules).

- ii. Patient has progressive or relapsed disease.

### **CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Coverage of everolimus products is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

### **REFERENCES**

1. Afinitor® tablets, Afinitor Disperz® tablets for oral suspension [prescribing information]. East Hanover, NJ: Novartis; February 2022.
2. Torpenz™ tablets [prescribing information]. Maple Grove, MN: Upsher-Smith; June 2024.
3. Zortress® tablets [prescribing information]. East Hanover, NJ: Novartis; January 2021.
4. The NCCN Drugs & Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 5, 2024. Search term: everolimus.